

## EXTENDED REPORT

# The influence of central corneal thickness and age on intraocular pressure measured by pneumotonometry, non-contact tonometry, the Tono-Pen XL, and Goldmann applanation tonometry

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**Aims:** To evaluate the influence of central corneal thickness (CCT) on intraocular pressure (IOP) measurements made with the Goldmann applanation tonometer (GAT), Tono-Pen XL, ocular blood flow tonograph (OBF), and Canon TX-10 non-contact tonometer (NCT).

**Methods:** CCT was recorded for either eye (randomly selected) of each of 105 untreated patients with ocular hypertension and glaucoma attending the glaucoma research unit at Moorfields Eye Hospital. For each of the selected eyes, IOP was measured with the GAT (two observers), Tono-Pen, OBF, and NCT in a randomised order. The relation of measured IOP and of inter-tonometer differences with CCT and subject age was explored by linear regression analysis.

**Results:** A significant association between measured IOP and CCT was found with each instrument. The change in measured IOP for a 10 µm increase in CCT was 0.28, 0.31, 0.38, and 0.46 for the GAT, Tono-Pen, OBF, and NCT, respectively (all  $p \leq 0.05$ ). There was a significant association between the NCT/GAT differences and CCT, with a tendency of NCT to overestimate GAT in eyes with thicker corneas. There was a significant association between GAT/Tono-Pen and OBF/Tono-Pen differences and age, with a tendency of GAT and OBF to overestimate the Tono-Pen in eyes of older subjects.

**Conclusion:** IOP measurement by all four methods is affected by CCT. The NCT is affected by CCT significantly more than the GAT. Subject age has a differential effect on the IOP measurements made by the GAT and OBF compared to the Tono-Pen.

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Central corneal thickness (CCT) is known to affect the accuracy of intraocular pressure (IOP) measurements by applanation tonometry.<sup>1,2</sup> A thicker cornea requires greater force to applanate and, conversely, a thinner cornea is more easily flattened. A thin cornea is a significant risk factor for the development of glaucoma<sup>3</sup> and it has yet to be determined whether this is an independent effect or a result of the influence of CCT on IOP measurements.

Most published studies concerning the effect of CCT on measured IOP relate to the Goldmann applanation tonometer (GAT). However, there is increasing evidence that other tonometers share this problem.<sup>4–6</sup> The GAT, Tono-Pen, ocular blood flow tonograph (OBF), and non-contact tonometer (NCT) all use an applanation principle. Thin shell theory was used by Orssengo and Pye to demonstrate that corneal radius, thickness and material stiffness affect the applanation pressure for a given IOP. Reducing the applanation area reduces the difference between the applanation pressure and IOP, because of the reduced resistance offered by the cornea for a smaller contact area.<sup>7</sup> There may also be some reduced effects from surface tension.

The GAT is based on the Imbert-Fick law,<sup>1,8</sup> which assumes that the cornea has a dry surface, is infinitely thin, and behaves as a "membrane" where the applanating pressure will equal the IOP. In practice, a resistance force, because of the thickness of the cornea, and a surface tension force, the result of the tear film, act upon the applanator causing this membrane assumption to be incorrect. These forces balance each other for the GAT (applanation diameter of 3.06 mm) when the CCT is 520 µm, providing a "reference" value where the applanating pressure does equal the IOP.<sup>1</sup>

The NCT uses a puff of air directed at the cornea with an applanation area, for the Canon TX-10, similar to that of the GAT. The force produced by the air puff is linearly increased over 8 ms and progressively flattens the cornea. When flat, the cornea acts as a mirror reflecting a light beam onto a sensor that triggers a reading. The Tono-Pen works on a principle similar to the MacKay-Marg tonometer<sup>9</sup> and has an applanation area smaller (2.36 mm<sup>2</sup>) than that of the GAT (7.35 mm<sup>2</sup>).<sup>10</sup> The OBF, or pneumatonometer, measures the pressure in a flowing column of gas (tonometer chamber) directed towards a thin membrane (diameter about 2.5 mm) in contact with the surface of the cornea. The probe tip has an outer diameter of about 5 mm. A portion of the gas flow pushes the outer part of the tonometer tip against the cornea, depressing its surface, and a portion maintains the pressure required to balance the pressure on the other side of the tip membrane (that is, the IOP) in the central part of the probe tip.<sup>11,12</sup> The probe tip applanates the cornea for about 5–10 seconds while a continuous IOP trace is recorded.

In the companion paper, we reported the level of agreement between IOP measurements made with the GAT, Tono-Pen XL, OBF, and Canon TX-10 NCT. The effect of CCT and subject age on tonometric measurements made with these four techniques is described in this paper. The study reported in this paper is the first to compare all four tonometric methods in the same eyes.

**Abbreviations:** CCT, central corneal thickness; DCT, dynamic contour tonometer; GAT, Goldmann applanation tonometer; IOP, intraocular pressure; NCT, non-contact tonometer; OBF, ocular blood flow; ORA, ocular response analyser

**Table 1** Association between measured intraocular pressure and central corneal thickness for each method, as determined by linear regression analysis

	Slope	95% CI for slope	Adjusted $R^2$	p Value
GAT 1	0.028	0.006 to 0.049	0.05	0.011
GAT 2	0.026	0.0002 to 0.051	0.04	0.033
Tono-Pen	0.031	0.010 to 0.053	0.07	0.004
OBF	0.038	0.009 to 0.068	0.05	0.012
NCT	0.046	0.022 to 0.070	0.12	0.000

## MATERIALS AND METHODS

Details of the study design, and materials and methods have been given in the companion paper. Table 1 of the companion paper lists patient data, CCT values and range of IOP measurements made with the four tonometers.

### Statistical analyses

Linear regression analysis was used to explore the relations between measured IOP and CCT and subject age and between tonometry inter-method differences and CCT and age. With 105 subjects, the study had a power of 80% at  $p = 0.05$  to detect a correlation of 0.245 ( $\equiv r^2 = 0.06$ ) between measured IOP and CCT (one sided test). Estimation of the effect of age was a post hoc analysis justified by suggestions in the literature that the cornea stiffens with age.<sup>13-15</sup>

The relation between tonometry inter-method differences and CCT and inter-method mean IOP was sought by stepwise multiple linear regression (CCT and IOP as the independent variables; probability of F to enter = 0.05 and to remove = 0.10).

## RESULTS

The association of measured IOP and CCT with each tonometer is summarised in table 1. The effect of CCT was least for the GAT and greatest for NCT, although the 95% confidence limits for the slopes overlapped for all four methods.

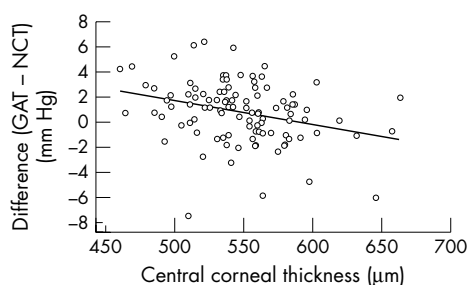
The GAT/NCT differences were significantly related to CCT for both GAT observers (see fig 1 for GAT observer 1); the equations were:

Observer 1:  $\text{GAT/NCT difference} = (-0.187 \times \text{CCT}) + 10.9$  (adjusted  $R^2 = 0.07$ ;  $p = 0.003$ )

Observer 2:  $\text{GAT/NCT difference} = (-0.199 \times \text{CCT}) + 12.0$  (adjusted  $R^2 = 0.08$ ;  $p = 0.002$ )

GAT/NCT differences were significantly related both to method mean IOP and to CCT for GAT observer 1 only; the equations were:

$\text{GAT/NCT difference} = (-0.129 \times \text{IOP}) + (-0.014 \times \text{CCT}) + 10.5$  (adjusted  $R^2 = 0.11$ ;  $p = 0.02$  for the IOP coefficient and  $p = 0.03$  for the CCT coefficient). Thus, the difference between GAT observer 1 and NCT increased both with the level of IOP and CCT.



**Figure 1** Differences between intraocular pressure measurements made with the Goldmann applanation tonometer by observer 1 and those made with the Canon TX-10 non-contact tonometer plotted against central corneal thickness.

OBF/NCT differences were also significantly related to IOP and CCT; the equation was:

$\text{OBF/NCT difference} = (-0.218 \times \text{IOP}) + (-0.018 \times \text{CCT}) + 6.7$  (adjusted  $R^2 = 0.12$ ;  $p = 0.0003$  for the IOP coefficient and  $p = 0.03$  for the CCT coefficient)

GAT/tonometer differences for other pairs of instruments were not related to CCT.

CCT and IOP measured by each tonometer were unrelated to subject age. However, GAT/Tono-Pen (fig 2) and OBF/Tono-Pen differences were significantly related to subject age; the equations were:

$\text{GAT/Tono-Pen difference} = (0.05 \times \text{age}) - 2.70$  (adjusted  $R^2 = 0.04$ ;  $p = 0.035$ )

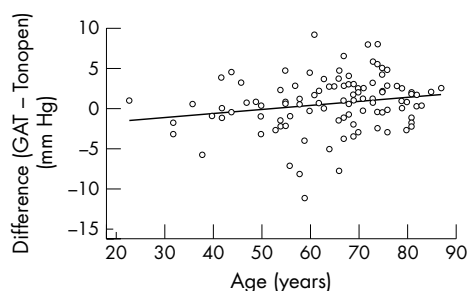
$\text{OBF/Tono-Pen difference} = (0.06 \times \text{age}) - 3.51$  (adjusted  $R^2 = 0.04$ ;  $p = 0.045$ )

## DISCUSSION

Several studies have examined the relation between IOP measured by various tonometers and CCT (table 2). The findings from an early study, in which eyes were cannulated and true IOP was measured with a manometer, showed an average tonometric (Perkins or Draeger) error of  $\pm 0.7$  mm Hg per 10  $\mu\text{m}$  deviation of CCT from the normal thickness of 520  $\mu\text{m}$ .<sup>1</sup> A lower average correction of 0.18–0.23 mm Hg per 10  $\mu\text{m}$  was observed by Whitacre *et al* in a similar in vivo study in 15 eyes with normal corneas.<sup>2</sup> This latter finding is close to that found in the present study. However, an association between applanation tonometry error (the difference between Tono-Pen or Perkins tonometer and manometric IOP) and CCT was not found by Felgen *et al*<sup>16</sup> or Foster *et al*.<sup>17</sup>

In general, there is good agreement between clinic based and population based studies of an increase in GAT measured IOP as CCT increases (table 2). The slope estimates in clinic based studies are slightly steeper than those in population based studies. This may result from a bias introduced by referral patterns, where tonometry is almost universally performed for glaucoma case finding.

NCT was significantly more susceptible to the effects of CCT than GAT, in accordance with previous findings.<sup>18-20</sup> The slope of the relation GAT/NCT difference versus CCT was



**Figure 2** Differences between intraocular pressure measurements made with the Goldmann applanation tonometer by observer 1 and those made with the Tono-Pen plotted against subject age.

**Table 2** Increase in IOP (mm Hg) for every 10 µm increase in CCT. Summary of previous findings regarding effect of CCT on IOP measurements

Author	Study type	Country	GAT	Tono-Pen	OBF	NCT
This study	Clinic based	United Kingdom	0.28	0.31	0.38	0.46
Ko <i>et al</i> , 2004 <sup>6</sup>	Clinic based	Taiwan	0.37		0.47	0.63
Siganos <i>et al</i> , 2004 <sup>36</sup>	Clinic based	Greece	0.26			0.39
Bhan <i>et al</i> , 2002 <sup>5</sup>	Clinic based	United Kingdom	0.23	0.10	0.28	
Gunvant <i>et al</i> , 2004 <sup>21</sup>	Clinic based	United Kingdom	0.27		0.48	
Morgan <i>et al</i> , 2003 <sup>12</sup>	Clinic based	United Kingdom			0.30	
Shimmyo <i>et al</i> , 2003 <sup>22</sup>	Clinic based	United States	0.16			
Eysteinnsson <i>et al</i> , 2002 <sup>23</sup>	Population based	Iceland				0.22 (M) 0.28 (F)
Dohadwala <i>et al</i> , 1998 <sup>4</sup>	Population based	Indian subcontinent		0.29 (M) 0.12 (F)		
Foster <i>et al</i> , 2003 <sup>24</sup>	Population based	Singapore	0.15 (R) 0.18 (L)			
Foster <i>et al</i> , 1998 <sup>25</sup>	Population based	Mongolia	0.18 (R) 0.24 (L)			
Wolfs <i>et al</i> , 1997 <sup>38</sup>	Population based	Netherlands	0.19			
Nemesure <i>et al</i> , 2003 <sup>39</sup>	Population based	Barbados	none			
Feltgen <i>et al</i> , 2001 <sup>16</sup>	Manometry	Germany	none			
Foster <i>et al</i> , 2000 <sup>17</sup>	Manometry	Singapore	none			
Ehlers, 1975 <sup>1</sup>	Manometry	Denmark	0.71			

M, male; R, right eye; F, female; L, left eye.

about -0.2 mm Hg per 10 µm, compared to -0.37 mm Hg per 10 µm reported by Graf.<sup>18</sup> In clinic and population studies, CCT explains between 1% and 6% of the variance in GAT measured IOP and 7% to 12% of the variance in NCT measured IOP.<sup>21-25</sup> A possible explanation of the greater effect of CCT on NCT measured IOP lies in the viscoelastic property of the cornea,<sup>26</sup> in which stiffness is related to the rate of application of strain. The cornea is deformed over about 8 ms, resulting in relatively greater stiffness than under the conditions of GAT, where IOP measurement is effectively static. Other possible explanations include the relative effects of ocular expansion in the rapid and slow applanation conditions and the effect of pressure waves reflected back and forth through the eye with rapid applanation. A new NCT, the ocular response analyser (ORA; Reichert Inc, Depew, NY, USA), exploits the viscoelastic properties of the cornea. The ORA measures two applanation events, one as the pressure in the air jet rises and one as it falls. There is a difference in pressure for the inward and outward applanation events—a property called hysteresis. Preliminary data suggest that the hysteresis value correlates well with CCT.<sup>27</sup>

We observed an overestimation of IOP by NCT relative to GAT and OBF at higher IOP levels. Possible explanations include a non-linear increase in corneal stiffness as IOP rises and corneal viscoelastic properties that are not accounted for by CCT. A small tonographic effect was seen with one of the GAT observers and with the OBF, so there may be a contribution from the effect of reduced aqueous outflow facility on measured IOP differences, the effect being greater on tonometry with very rapid flattening of the cornea.

The finding in this study of an increase in IOP measured by the Tono-Pen of 0.31 mm Hg per 10 µm increase in CCT is greater than previously reported figures of 0.19 mm Hg/10 µm<sup>4</sup> and 0.10 mm Hg/10 µm<sup>5</sup> (table 2), although the confidence intervals for the estimate are wide (table 1). It is thought that the Tono-Pen may be less affected by CCT than the GAT because it applanates a smaller area of the cornea.<sup>7 10</sup>

Walker and Litovitz<sup>28</sup> proposed that IOP measurements by pneumotonometry would be little affected by CCT as flexural rigidity could be ignored, because the outer edges of the probe flatten the cornea and the tension forces, by which IOP is measured, occur under the central portion of the probe. However, this and other studies have reported a dependence of OBF measured IOP on CCT.<sup>5 12 21 29</sup> An explanation is

provided by Morgan *et al*.<sup>12</sup> A portion of the air flow of the pneumotonometer holds the probe against the cornea to provide the initial corneal flattening and is susceptible to the effects of the CCT.

The results of a re-analysis of published data demonstrated that a 10% difference in CCT results in a difference of 1.1 (SD 0.6) mm Hg in IOP measurements,<sup>30</sup> equivalent to a change of 0.20 mm Hg for every 10 µm change in CCT. This result is supported by more recent findings (table 2). The validity of this relation is based on the assumption of a linear dependence of measured IOP on CCT, and on the absence of a relation between true IOP and CCT. Ehlers *et al* found a significant (p<0.001) correlation between the error of GAT IOP readings and CCT. However, the relation was non-linear, and IOP measurements required correction for CCT in relation to true IOP.<sup>1</sup> The latter findings were confirmed by Orssengo and Pye, who demonstrated that the modulus of elasticity of the cornea was related to true IOP.<sup>7</sup>

Opinion is divided about the clinical significance of the effect of CCT on IOP measurements. Singh *et al* suggested that the effect was small and probably not relevant for most patients.<sup>29</sup> Conversely, a recent report suggested that a correction for corneal effects might be needed for some groups of patients.<sup>5</sup> In a literature review, Doughty and Zaman reported a mean CCT of 544 (SD 34) µm for measurements made by ultrasound pachymetry.<sup>30</sup> From this, 95% of corneas should have a CCT in the range 477-611 µm. If a value of 0.20 mm Hg IOP increase per 10 µm increase in CCT is assumed,<sup>30</sup> then the CCT could account for a difference in measured IOP of 2.7 mm Hg between the thickest and the thinnest corneas. One in 20 eyes will fall outside these extremes. Although this difference may be quite small in relation to the GAT measurement error, the distribution of CCT values in clinic populations is unlikely to reflect that of the general population. Falsely high IOP readings made (especially by NCT) in the community will lead to a concentration of thicker corneas in clinic populations. Thus, CCT measurement is useful to identify normal eyes falsely classified as ocular hypertensive. Similarly, the classification of eyes on the basis of IOP as normal or high tension glaucoma inevitably leads to a relatively greater proportion of eyes with thin corneas in the normal tension group.

The cornea is thought to stiffen with age<sup>13</sup> as a result of ultrastructural changes in the collagen fibrils of the corneal stroma.<sup>14 15</sup> The finding of a significant relation between GAT/

Tono-Pen (fig 2) and OBF/Tonopen differences and subject age, with GAT and OBF overestimating IOP relative to the Tono-Pen in older subjects, may be explained by a stiffer cornea in older subjects, if Tono-Pen IOP measurements are less dependent on the biomechanical properties of the cornea. An effect of a reduced tear film may contribute. Eisenberg *et al*<sup>31</sup> measured IOP by manometry, Perkins tonometry, pneumotonometer, and the Tono-Pen in nine subjects aged from 0.1 to 85 years. There was a significant effect of subject age on Perkins IOP measurement error, but not on the measurement error of the Tono-Pen and pneumotonometer. The Perkins overestimated the Tono-Pen at older ages. The magnitude of the effect in present study was a relative increase in measured IOP (by GAT or OBF over the Tono-Pen) of about 0.5 mm Hg per decade, or 3.2 mm Hg across the age range of subjects in the study.

The effect of corneal biomechanics on IOP measurement is a research area that is gaining importance, given the increasing prevalence of individuals having undergone corneal refractive surgery. Stromal thinning following refractive procedures has been demonstrated to result in changes in IOP measured by the GAT, NCT, and Tono-Pen.<sup>32-34</sup> A new method of tonometry, the Pascal dynamic contour tonometer (DCT; Ziemer Ophthalmic Systems AG, Port Switzerland), is said not to be affected by corneal biomechanical properties. The applanation tip has a concave surface (radius of curvature 10.5 mm) with an embedded pressure sensor and, when contour matching between the tonometer tip and the cornea is achieved, the mechanical properties of the cornea do not contribute to the IOP measurement. Two studies have reported that DCT measured IOP is independent of CCT<sup>35 36</sup> and studies on patients undergoing laser corneal refractive surgery have demonstrated that, unlike GAT IOP measurements, Pascal IOP measurements are unaltered by the laser surgery.<sup>36 37</sup>

In conclusion, the findings of the present study demonstrate that IOP measurements by the GAT, Tono-Pen, OBF, and NCT are all significantly influenced by CCT, and that the effect of CCT on NCT is significantly greater than on the GAT.

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